Docket No.: PF-0442-2 RCE

REMARKS

Claims 1, 2, 4, 5, 9, 10, 12, 16-19 and 22-23 have previously been canceled without prejudice or disclaimer.

Claims 50-51 were submitted in Applicants' Amendment filed June 3, 2003 in response to the Final Office Action mailed April 24, 2003, but were not entered.

By this amendment, claims 40-49 are canceled without prejudice or disclaimer, and claims 52-53, drawn to a method of using the claimed polynucleotides, and claim 53, drawn to a polynucleotide, are added. New claim 52 is directed to subject matter originally encompassed by original claim 9; new claim53 is identical to original claim 23. Both find support in the specification and the claims as originally filed, and therefore no new matter is added to this application by their inclusion.

Claim 20 was withdrawn from consideration pursuant to Applicants' election of the claims of Group II in their Response to the Restriction Requirement mailed May 13, 2002, which response was filed on June 13, 2002.

Therefore, claims 3, 6-8, 11, 13-15, 20-21 and 52-53 are currently pending.

Claims 3, 6-8, 11, 13-15, 21 and 50-51 are currently under consideration in this application.

The Final Rejections as presented in the Final Office Action of April 24, 2003 indicated that claim 11 was directed to an allowable product, and that in light of the allowable product claim, claims 13-15 and 21, directed to methods of making and using the polynucleotides recited in claim 11 would be rejoined and examined pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86).

In Applicants' Response to Final, filed June 3, 2003, Applicants attempted to amend subsection (d) of claim 3, directed to immunogenic fragments of SEQ ID NO:1, by adding the further limitations that the fragment be at least 5 amino acids in length, and that the fragment is used to make an antibody which specifically binds to an isolated polypeptide selected from the group consisting of a), b) and c) of claim 3. Applicants also attempted to add new claims 50 and 51, directed, respectively, to a method of producing the polypeptides of [canceled] claim 3, and to a method of producing the polypeptide comprising the amino acid sequence of SEQ ID NO:1.

The Advisory Action of July 8, 2003 indicated the Examiner's refusal to enter the Amendment After Final. She reasoned that adding new claims 50 and 51 would require further

consideration and/or further search, both because they depended from claim 3, which had previously been canceled, and because they were directed towards a method of polypeptide production despite Applicants' previous election of claims directed to polynucleotides.

The Examiner also did not enter the amendment to claim 3(d), and maintained the rejection of claims 3 and 6-8 under 35 U.S.C. § 112, first paragraph pertaining to immunogenic fragments of SEQ ID NO:1 recited in subsection (d) of claim 3; however, she indicated that Applicants' amendment, if entered, would have overcome the written description rejection of claims 3 and 6-8 under 35 U.S.C. §112, first paragraph as to those fragments.

Rejoinder of Method Claims

Applicants reiterate that upon allowance of any of the product claims (claims 3, 6, 7, 11, 53), there should be rejoinder of "method of use" claims 8, 13-15, 20-21 and 52, in accordance with the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)."

Amendments to the Claims

Claim 3 has been amended in order to further define the claimed invention. In particular, claim 3 b) has been amended to remove recitation of "said polypeptide having cyclic nucleotide phosphodiesterase activity." Applicants intent is to restore claim 3 b) to its original form, owing to the fact that polynucleotides which encode nonfunctional polypeptides are likely to be associated with disease states and provide a method to identify said disease states.

Claim 3 d) has also been amended to include the recitation of "an immunogenic fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1, said immunogenic fragment is used to make an antibody which specifically binds to an isolated polypeptide selected from the group consisting of a), b) and c)." Support for this amendment can be found throughout the specification, e.g., p. 8, lines 16-19, p. 9, line 28, through page 10, line 1, page 30, lines 7-9 and page 52, lines 25-28. No new matter is added by this amendment. It is believed that entry of the requested amendment is proper.

Applicants note that the amendment to claim 3 d) is identical to the one submitted in their Response to the Final Office Action, filed June 4, 2003.

Claim 11 b) has been amended to remove recitation of "encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:1 and said polypeptide having cyclic nucleotide phosphodiesterase activity." Again, Applicants' intent is to restore claim 11 b) to its original form, for the reason supporting the amendment to claim 3 b) stated above.

Claim 52 has been added to capture use of a polynucleotide of claim 11 in the method of claim 8 to produce a polypeptide having the sequence of SEQ ID NO:1; this method was previously encompassed by original claim 9 (now canceled). Support for this amendment can be found throughout the Specification, e.g., page 20, lines 3-29, and in claim 9 as originally filed. No new matter is added thereby.

Claim 52 has been added to claim the subject matter of original claim 23 (now canceled). No new matter is added thereby.

Written Description Rejection Under 35 U.S. C. § 112, first paragraph

Claims 3 and 6-8 stand rejected under U.S.C. § 112, first paragraph, for the reason given at page 3 of this Office Action. Applicants traverse this rejection for the reasons that follow.

A. Legal Requirements

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a

> skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. (Footnotes omitted)

Moreover, according to the Manual of Patent Examining Procedure, evaluation of the Specification's disclosure showing that applicant was in possession of the claimed invention is a multi-factorial determination.

> Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. (M.P.E.P. 2163 II. A. 3. (a) i) (C) (2), emphasis added).

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

B. The Specification provides an adequate written description of the claimed "immunogenic" term as it relates to fragments of SEQ ID NO:1

The subject matter encompassed by claims 3 and 6-8 is adequately disclosed in the Specification given what is conventional or well known to one skilled in the art.

Please note that the "immunogenic" language of independent claim 3 as amended recites:

> 3. **(Three Times Amended)** An isolated polynucleotide encoding a polypeptide selected from the group consisting of: . . .
>
> d) an immunogenic fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1, said immunogenic fragment is used to make an antibody which specifically binds to an isolated polypeptide selected from the group consisting of a), b) and c).

Applicants submit that the Specification provides an adequate written description of the claimed polynucleotide encoding a polypeptide consisting of an "immunogenic" fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1 to convey with

reasonable clarity to those skilled in the art that applicant was in possession of the invention as claimed at the time of the filing of this application.

The Examiner's position is that although the Specification provides an adequate written description of the polypeptide of SEQ ID NO:1, fragments and 90-99% variants thereof as well as the polynucleotide of SEQ ID NO:2, fragments and 90-99% variants thereof, adequate written description of "immunogenic" is lacking (Office Action of April 29, 2003 at pages 2-3). Applicants strongly disagree with this position.

The structure of the "immunogenic" fragments is defined in terms of the amino acid sequence of the SEQ ID NO:1 (PDE9A) polypeptide and fragments thereof to which antibodies would be made and specifically bind. The Specification defines and one of skill in the art understands "immunogenic" fragments as those fragments which have the capability to be "immunologically active . . . the capability of the natural, recombinant, or synthetic PDE9A, or any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies" (Specification, page 9, line 28 through page 10, line 1).

The Specification teaches SEQ ID NO:1 as provided in Figures 1A-1F, 2A-2D and in the Sequence Listing, pages 54-56. Moreover, methods of identifying immunogenic regions and so, immunogenic fragments of SEQ ID NO:1 are also provided in the Specification. Specifically, the DNASTAR software suite includes the LASERGENE program. Such software programs are well known to one of ordinary skill in the art and are routinely used to identify antigenic ("immunogenic") regions, including "an immunogenic" fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1" (See, for example, Example XI, pages 52-53). Given the information provided by SEQ ID NO:1 (the amino acid sequence of PDE9A) and SEQ ID NO:2 (the polynucleotide sequence encoding PDE9A), one of skill in the art would be able to routinely obtain "an immunogenic fragment of at least 5 amino acids of a polypeptide having the amino acid sequence of SEQ ID NO:1" as recited in claim 3. Further, the skilled artisan knows that within the protein or fragments thereof which are used to immunize a host animal there exist numerous regions (the immunogenic (antigenic) fragments) which may induce the production of antibodies.

Additionally, the Specification teaches methods of making antibodies using oligopeptides, peptides, or fragments of PDE9A which consist of at least 5 amino acids of SEQ ID NO:1 (See, for example, page 29, line 25 through page 31, line 10 and Example XI, pages 52-

53). Thus, one skilled in the art need not make and test vast numbers of "immunogenic" fragments of SEQ ID NO:1. Instead, one of skill in the art need only analyze the polypeptide sequence of SEQ ID NO:1 for "immunogenic" regions, as described above. Further, because the art is very advanced, it is well known to one of skill in the art that antibody production requires routine experimentation in order to determine which "immunogenic" regions of a polypeptide or fragment thereof, result in an antibody with the desired antipeptide activity. The Specification also provides an assay (Example XI) for optimizing selection of immunogenic fragments of SEQ ID NO:1 used to make PDE9A specific antibodies. Likewise, the Examiner should note and one of skill in the art would recognize that antibodies made from such "immunogenic" fragments of SEQ ID NO:1 which specifically bind to the PDE9A polypeptide can be used to purify PDE9A from media containing PDE9A as taught in Example XII (page 53). Therefore, Applicants have provided an adequate written description of "immunogenic" fragments of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1 in terms of the structure of SEQ ID NO:1, use of sequence analysis programs well known to one of skill in the art and assays for producing and testing antibodies made with said "immunogenic" fragments (Examples XI and XII).

When provided with the detailed description as noted above, one of ordinary skill in the art "would have understood the inventor to be in possession of the claimed invention at the time of filing." That is, given the polypeptide sequence of SEQ ID NO:1 and the appropriate software program for the analysis of antigenic regions of a polypeptide, it would be routine for one of skill in the art to recognize whether a fragment of a polypeptide of SEQ ID NO:1 was "immunogenic." Accordingly, the Specification, together with what is conventional or well known to one of ordinary skill in the art, provides an adequate written description of "an immunogenic fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1."

Applicants submit that "a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing" as stated in the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001. Accordingly, claims 3 and 6-8 meet the statutory requirements for written description under 35 U.S.C. 112, first paragraph. For at least the above reasons it is requested that this rejection be withdrawn.

C. Conclusion

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an analysis of the present claims. In particular, the "immunogenic" fragments of SEQ ID NO:1 are adequately described, as evidenced by the advanced nature of the art, the skill of the ordinary artisan and the specific passages of the Specification as set forth above. In addition, the Office Action of August 29, 2002 provided no analysis of why one of ordinary skill in the art would not have understood from the disclosure in the Specification along with "[w]hat is conventional or well known to one of ordinary skill in the art," that Applicants were in possession of "immunogenic" fragments of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1.

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CONCLUSION

In light of the REQUEST FOR CONTINUED EXAMINATION (RCE) request, and the above amendments and remarks, Applicants request Continued Examination of the present application, and request that prosecution be directed to claims to **polynucleotides**. They further request that the claim amendments and new claims presented above be entered.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicant's Agent at (650) 621-8555.

The Commissioner is hereby authorized to charge Deposit Account No. 09-0108 the amount of $750.00 as set forth in the accompanying transmittal letter. If the Commissioner determines that additional fees are due or that an excess fee has been paid, the Patent Office is authorized to debit or credit (respectively) Deposit Account No. **09-0108**.

Respectfully submitted,

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Comments:

RCE Transmittal and Preliminary Amendment for the above identified Patent Application.